II. REMARKS

Formal Matters

Claims 1 and 3-24 are pending after entry of the amendments set forth herein.

Claims 1-17 were examined and were rejected.

Claims 1, 3, and 4 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. Claims 3 and 4 are amended to depend from claim 1; as such, no new matter is added by the amendments to claims 3 and 4. Support for the amendments to claim 1 is found in the claims as originally filed (e.g., originally filed claim 2), and throughout the specification, in particular at the following exemplary locations: paragraphs 0038, 0041, and 0043. Accordingly, no new matter is added by the amendments to claim 1.

Claim 2 is canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claim. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Claims 18-24 are added. Support for new claims 18-24 is found in the claims as originally filed, and throughout the specification, including the following exemplary location: claim 18: paragraph 0011; claim 19: paragraph 0039; claims 20 and 21: paragraph 0057; claim 22: paragraph 0059; claims 23 and 24: paragraph 0060. Accordingly, no new matter is added by new claims 18-24.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Claim objection

Claim 1 was objected to. The Office Action stated that the claim is directed to a nucleic acid that exists in nature and not to an isolated nucleic acid or a nucleic acid encoding a gene product.

Applicants note that claim 1 is not directed to a nucleic acid. Instead, claim 1 recites a method of treating irritable bowel syndrome (IBS) in an individual, the method comprising administering to the individual an effective amount of a therapeutic nucleic acid to reduce at least one symptom of IBS in the individual. As such, claim 1 need not be amended.

Nonstatutory double patenting

Claims 1, 2, 5, 7, and 8 were rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1 and 9-14 of U.S. Patent No. 6,613,751. Applicants respectfully traverse the rejection.

U.S. Patent No. 6,613,751 claims a method of treating gastrointestinal inflammation. The instant claims are directed to methods of treating irritable bowel syndrome (IBS). IBS is not the same as gastrointestinal inflammation. A method of treating IBS is not an obvious variation of a method of treating gastrointestinal inflammation.

As discussed in the instant specification, IBS is a functional bowel disorder for which there is currently no mechanical, biochemical, or overt inflammatory condition that explains the symptoms. Specification, paragraph 0004. Indeed, according to the National Institutes for Health, inflammation is not a feature of IBS. As such, IBS is a disorder that is distinct from "gastrointestinal inflammation." In keeping with this distinction, U.S. Patent No. 6,613,751 does not include IBS among the list of gastroinflammatory disorders.

Furthermore, treatment of IBS is not obvious in view of treatment of "gastrointestinal inflammation." Current treatments for IBS include medications to treat constipation or diarrhea; antidepressants; and anticholinergic medications. Such medications are typically not used for treating gastrointestinal inflammatory disorders such as inflammatory bowel disease (IBD), Crohns' disease, and ulcerative colitis. Instead, gastrointestinal inflammatory disorders are typically treated with anti-inflammatory agents such as anti-inflammatory steroidal compounds. Conversely, in keeping with the fact that IBS is not an inflammatory disorder, anti-inflammatory agents such as anti-inflammatory steroidal compounds are typically not used for treating IBS.

IBS is not the same as gastrointestinal inflammation. A method of treating IBS is not an obvious variation of a method of treating gastrointestinal inflammation. As such, this rejection of claims 1, 2, 5, 7, and 8 may be withdrawn.

Rejection under 35 U.S.C. §112, first paragraph

Claims 1-17 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement.

The Office Action stated that the specification "fails to provide any guidance and/or working examples or any data at all for administering any nucleic acid at an effective level for treating IBS." Office Action, bridging sentence, pages 2-3. Applicants respectfully traverse the rejection.

The Office Action stated that "one of skill in the art could not rely on the state of the gene therapy art to treat IBS by way of the claimed methods." Office Action, page 3.

However, the instant claims do not relate to "gene therapy." As explained in the instant specification, therapeutic nucleic acids suitable for use in a subject method generally do not provide for expression of any amino acid sequence encoded by the polynucleotide. Specification, paragraph 0038. As such, the statement that "one of skill in the art could not rely on the state of the gene therapy art to treat IBS by way of the claimed methods" is irrelevant to the instant methods as claimed.

The Office Action asserted that "the art teaches that for example administration of 5'-CG-3' is unpredictable" and that "the therapeutic efficacy of 5'-CpG-3' nucleic acid treatment of IBS is unpredictable." Office Action, page 4 and page 5. To support this assertion, the Office Action cited:

Barbara et al. ((2002) *Gut* 51:i41; "Barbara");

Shanahan ((2005) *Am. J. Physiol. Gastrointest. Liver Physiol.* 288:G417; "Shanahan"); and

Watson and McKay (2006) *Clinica Chimica Acta* 364:1; "Watson").

Barbara

Barbara does not teach that "administration of 5'-CG-3' is unpredictable." Instead, Barbara reviews references that explore the hypothesis on the role of low grade inflammation in IBS. Barbara does not even mention the possibility of using a therapeutic nucleic acid in the treatment of IBS. As such, Barbara does not support the assertion that "the art teaches that for example administration of 5'-CG-3' is unpredictable."

Shanahan

The Office Action stated that Shanahan teaches that in certain murine models of IBD, bacterial CpG DNA mediates the anti-inflammatory effect by signaling through host TLR9 receptors.

As explained above, IBS is **not the same condition** as IBD. Shanahan relates to IBD. As such,

in contrast to the Office Action's assertion, Shanahan does not teach that "therapeutic efficacy of 5'-CpG-3' nucleic acid treatment of IBS is unpredictable."

Watson

The Office Action cited passages in Watson in which various aspects of CpG ODNs were discussed. The Office Action's conclusory statement "Thus, the therapeutic efficacy of 5'-CpG-3' nucleic acid treatment of IBS is unpredictable" does not follow logically from the cited passages. The cited passages merely discuss considerations such as methylation of bacterial DNA. It does not follow from the cited passages that "the therapeutic efficacy of 5'-CpG-3' nucleic acid treatment of IBS is unpredictable."

Watson does not specifically discuss the effect of a therapeutic nucleic acid comprising the sequence 5'-CG-3' on treating IBS. Watson reviews the literature relating to 5'-CG-3' in treating gastroinflammatory disorders such as IBD, Crohn's disease, etc. As explained above, gastroinflammatory disorders are not the same as IBS. As such, Watson does not teach that "therapeutic efficacy of 5'-CpG-3' nucleic acid treatment of IBS is unpredictable."

The Office Action stated that "the instant specification does not provide any relevant teachings, specific guidance, or working examples for overcoming the limitations of route and dose of administration of a therapeutic nucleic acid for effective IBS therapy raised by the state of the art." Office Action, bridging sentence, pages 5-6.

First, as discussed above, the cited art does not teach that "therapeutic efficacy of 5'-CpG-3' nucleic acid treatment of IBS is unpredictable."

Secondly, the instant specification provides ample disclosure such that those skilled in the art could carry out a subject method without undue experimentation. The instant specification states that a therapeutic nucleic acid can be administered to a subject prior to the onset of symptoms (e.g., prior to abdominal pain, or after onset of symptoms (e.g., after onset of abdominal pain, after onset of constipation, after onset of diarrhea). Specification, paragraph 0022. The instant specification states that animal models of IBS are known in the art. Specification, paragraph 0021. The instant specification describes how to determine efficacy of a therapeutic nucleic acid in treating IBS. The instant specification states that the Rome criteria can be used, and provides a reference that describes the Rome

criteria. Specification, paragraph 0019. The instant specification states that effective amounts of a therapeutic nucleic acid are amounts that are effective to reduce at least one symptom of IBS, e.g., abdominal pain, constipation, and diarrhea. Specification, paragraph 0018. The specification states that exemplary effective amounts of a therapeutic nucleic acid are in the range of from about 1 μg to about 500 mg. Specification, paragraphs 0030-0034 and paragraph 0076. Furthermore, the specification provides ample guidance as to particular sequence motifs present in a therapeutic nucleic acid. Specification, paragraphs 0043-0064. In view of the ample description in the specification, and the knowledge in the art, those skilled in the art could readily carry out a claimed method without undue experimentation.

Thirdly, compliance with the enablement requirement under 35 U.S.C. §112, first paragraph, does not require or mandate that a working example be disclosed. The specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art would be able to practice the invention without undue experimentation.[1] Furthermore, "Nothing more than objective enablement is required, and therefore it is irrelevant whether [a] teaching is provided through broad terminology or illustrative examples."[2]

In sum, the amount of experimentation required to carry out a claimed method would not be undue because a) ample guidance is given on how to test the sequences, c) there is a good correlation between the activities of species within a genus of this breath, and d) one of skill in the art would be able to perform the experiments as a matter of routine to determine the active sequences.

The specification therefore provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation.

Conclusion as to the rejection under 35 U.S.C. §112, first paragraph

Applicants submit that the rejection of claims 1-17 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully

[1] In re Borkowski, 164 USPQ 642,645 (CCPA 1970).
[2] *In re Robins* 166 USPQ 552 at 555 (CCPA 1970).

requested to withdraw the rejection.

Rejection under 35 U.S.C. §102(b)

Claims 1, 14, 15, and 17 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Vesely et al. (U.S. Patent No. 5,716,615; "Vesely").

The Office Action stated that Vesely teaches a method for prophylaxis or treatment of gastrointestinal disorders comprising oral administration of bacteria.

Claim 1 as amended recites that the therapeutic nucleic acid is "isolated or synthetic." Vesely neither discloses nor suggests a method as recited in claim 1, comprising administering a therapeutic nucleic acid that is isolated or synthetic.

Conclusion as to the rejection under 35 U.S.C. §102(b)

Applicants submit that the rejection of claims 1, 14, 15, and 17 under 35 U.S.C. §102(b) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCSD-314.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: January 9, 2009

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